



## MT-ND1 gene

mitochondrially encoded NADH:ubiquinone oxidoreductase core subunit 1

### Normal Function

The *MT-ND1* gene provides instructions for making a protein called NADH dehydrogenase 1. This protein is part of a large enzyme complex known as complex I, which is active in mitochondria. Mitochondria are structures within cells that convert the energy from food into a form that cells can use. These cellular structures produce energy through a process called oxidative phosphorylation, which uses oxygen and simple sugars to create adenosine triphosphate (ATP), the cell's main energy source.

Complex I is one of several enzyme complexes necessary for oxidative phosphorylation. Within mitochondria, these complexes are embedded in a tightly folded, specialized membrane called the inner mitochondrial membrane. During oxidative phosphorylation, mitochondrial enzyme complexes carry out chemical reactions that drive the production of ATP. Specifically, they create an unequal electrical charge on either side of the inner mitochondrial membrane through a step-by-step transfer of negatively charged particles called electrons. This difference in electrical charge provides the energy for ATP production.

Complex I is responsible for the first step in the electron transport process, the transfer of electrons from a molecule called NADH to another molecule called ubiquinone. Electrons are then passed from ubiquinone through several other enzyme complexes to provide energy for the generation of ATP.

### Health Conditions Related to Genetic Changes

#### Leber hereditary optic neuropathy

Several mutations in the *MT-ND1* gene are known to cause Leber hereditary optic neuropathy. Each of these mutations changes a single DNA building block (nucleotide) in the gene. One common *MT-ND1* mutation is responsible for about 13 percent of all cases of Leber hereditary optic neuropathy. This mutation replaces the nucleotide guanine with the nucleotide adenine at gene position 3460 (written as G3460A). This change is associated with moderately severe cases of Leber hereditary optic neuropathy; however, 20 percent to 40 percent of people with vision loss due to this mutation experience some recovery of vision.

Researchers are investigating how mutations in the *MT-ND1* gene lead to Leber hereditary optic neuropathy. These genetic changes appear to disrupt the normal activity of complex I in the mitochondrial inner membrane, which may affect the generation of ATP. *MT-ND1* mutations also may increase the production within

mitochondria of potentially harmful molecules called reactive oxygen species. It remains unclear, however, why the effects of these mutations are often limited to the nerve that relays visual information from the eye to the brain (the optic nerve). Additional genetic and environmental factors probably contribute to the vision loss and other medical problems associated with Leber hereditary optic neuropathy.

### Leigh syndrome

#### mitochondrial encephalomyopathy, lactic acidosis, and stroke-like episodes

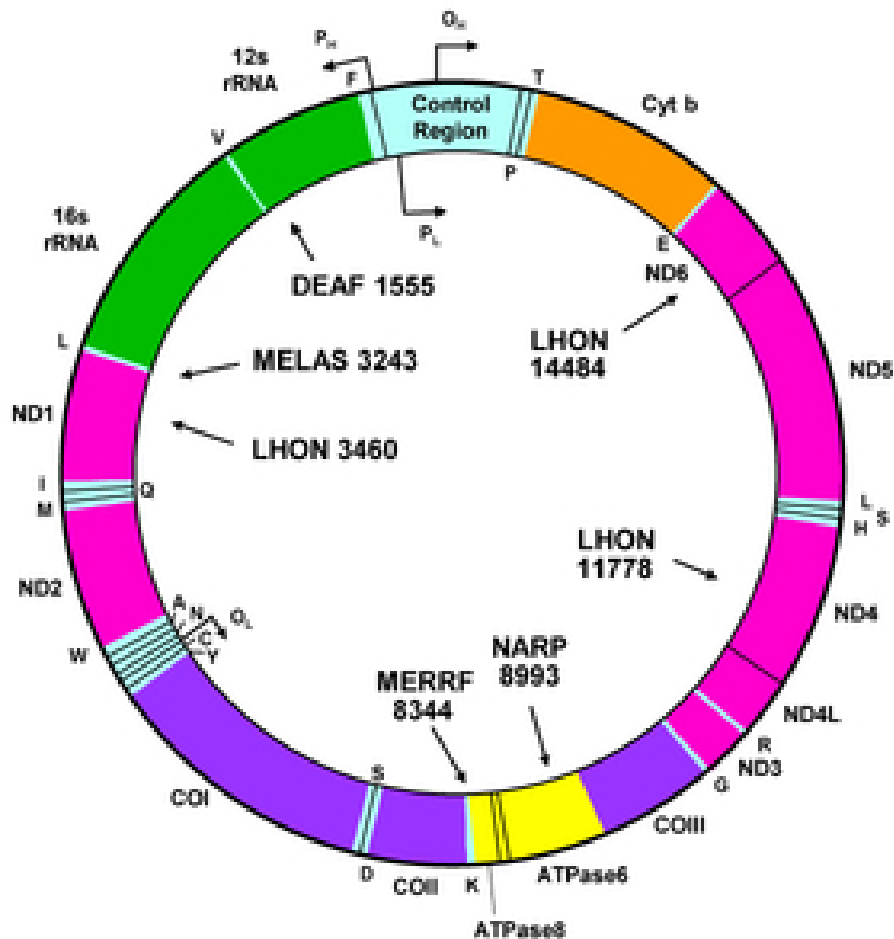
*MT-ND1* mutations are a rare cause of mitochondrial encephalomyopathy, lactic acidosis, and stroke-like episodes (MELAS). Most cases of MELAS are caused by mutations in other mitochondrial genes, but a small number of cases resulting from mutations in the *MT-ND1* gene have been reported. Fewer than five mutations, each of which alters a single DNA building block (nucleotide) in the gene, have been identified in affected individuals. These genetic changes reduce the activity of complex I, which disrupts energy production within mitochondria. Although these abnormalities have the greatest impact on tissues that require a lot of energy (such as the brain and muscles), researchers have not determined how changes in the *MT-ND1* gene lead to the specific signs and symptoms of MELAS.

### other disorders

A mutation in the *MT-ND1* gene has been reported in a few cases of adult-onset dystonia. Dystonia is a movement disorder that involves involuntary tensing of the muscles (muscle contractions), tremors, and other uncontrolled movements. The *MT-ND1* mutation associated with these rare cases replaces the nucleotide adenine with the nucleotide guanine at gene position 3796 (written as A3796G). Further studies are needed to determine whether this genetic change combines with other genetic and environmental factors to increase the risk of developing adult-onset dystonia.

## Chromosomal Location

Molecular Location: base pairs 3,307 to 4,262 on mitochondrial DNA (Homo sapiens Annotation Release 108, GRCh38.p7) (NCBI)



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## Other Names for This Gene

- mitochondrially encoded NADH dehydrogenase 1
- MTND1
- NADH dehydrogenase 1
- NADH dehydrogenase subunit 1

- NADH-ubiquinone oxidoreductase chain 1
- NADH-ubiquinone oxidoreductase, subunit ND1
- ND1
- NU1M\_HUMAN

## **Additional Information & Resources**

### Educational Resources

- Basic Neurochemistry (sixth edition, 1999): Diseases of Mitochondrial Metabolism  
<https://www.ncbi.nlm.nih.gov/books/NBK27914/>
- Biochemistry (fifth edition, 2002): Oxidative Phosphorylation  
<https://www.ncbi.nlm.nih.gov/books/NBK21208/>
- Mayo Clinic Mitochondrial Disease Biobank  
<http://www.mayo.edu/research/centers-programs/mitochondrial-disease-biobank/overview>
- The Neuromuscular Disease Center at Washington University: Complex I  
<http://neuromuscular.wustl.edu/pathol/diagrams/mito.htm#complexI>

### GeneReviews

- Leber Hereditary Optic Neuropathy  
<https://www.ncbi.nlm.nih.gov/books/NBK1174>
- MELAS  
<https://www.ncbi.nlm.nih.gov/books/NBK1233>
- Mitochondrial Disorders Overview  
<https://www.ncbi.nlm.nih.gov/books/NBK1224>

### Scientific Articles on PubMed

- PubMed  
<https://www.ncbi.nlm.nih.gov/pubmed?term=%28%28MT-ND1%5BTIAB%5D%29+OR+%28mitochondrially+encoded+NADH+dehydrogenase+1%5BTIAB%5D%29%29+OR+%28%28MTND1%5BTIAB%5D%29+OR+%28NADH+dehydrogenase+subunit+1%5BTIAB%5D%29+OR+%28NADH+dehydrogenase+1%5BTIAB%5D%29+OR+%28NADH-ubiquinone+oxidoreductase+chain+1%5BTIAB%5D%29+OR+%28NADH-ubiquinone+oxidoreductase,+subunit+ND1%5BTIAB%5D%29+OR+%28ND1%5BTIAB%5D%29%29+AND+%28%28Genes%5BMH%5D%29+OR+%28Genetic+Phenomena%5BMH%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+720+days%22%5Bdp%5D>

## OMIM

- COMPLEX I, SUBUNIT ND1  
<http://omim.org/entry/516000>

## Research Resources

- Atlas of Genetics and Cytogenetics in Oncology and Haematology  
[http://atlasgeneticsoncology.org/Genes/GC\\_ND1.html](http://atlasgeneticsoncology.org/Genes/GC_ND1.html)
- ClinVar  
<https://www.ncbi.nlm.nih.gov/clinvar?term=MT-ND1%5Bgene%5D>
- HGNC Gene Family: NADH:ubiquinone oxidoreductase core subunits  
<http://www.genenames.org/cgi-bin/genefamilies/set/1149>
- HGNC Gene Symbol Report  
[http://www.genenames.org/cgi-bin/gene\\_symbol\\_report?q=data/hgnc\\_data.php&hgnc\\_id=7455](http://www.genenames.org/cgi-bin/gene_symbol_report?q=data/hgnc_data.php&hgnc_id=7455)
- Mitomap: Coding and control region mutations  
<http://www.mitomap.org/MITOMAP/MutationsCodingControl>
- Mitomap: Leber hereditary optic neuropathy disease mutation database  
<http://www.mitomap.org/MITOMAP/MutationsLHON>
- NCBI Gene  
<https://www.ncbi.nlm.nih.gov/gene/4535>
- UniProt  
<http://www.uniprot.org/uniprot/P03886>

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Reprinted from Genetics Home Reference:  
<https://ghr.nlm.nih.gov/gene/MT-ND1>

Reviewed: November 2006  
Published: March 21, 2017

Lister Hill National Center for Biomedical Communications  
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